REMARKS

Claims 1-18 and 21-24 will be pending upon entry of the present amendment (claims 19-20 having been canceled and new claims 23 and 24 having been added). New **claims 23 and 24** are supported by, for example, original claim 8. Claims 2-18 and 22 have been amended for grammatical reasons, to include the simpler phrase "of claim X" rather than "according to claim X" and, in some cases, to perfect antecedent basis. No new matter has been added.

35 U.S.C. § 112, ¶ 2

Claims 1-22 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. More specifically, the Examiner states, "[t]he words 'reaction product' do not *explicitly state* the nature of the chemical reaction (whether electrovalent or covalent reaction) that takes place between an alkaloid and phosphate derivative of 'electron transfer agent'" (Office action at page 2; emphasis added).

Applicants maintain that the term "reaction product" is sufficiently clear. The Examiner is asked to reconsider this ground for rejection, particularly in view of the requirement for reasonableness. According to the MPEP at 2173.02, "When the examiner is satisfied that patentable subject matter is disclosed, and it is apparent to the examiner that the claims are directed to such patentable subject matter, he or she should allow claims which define the patentable subject matter with a reasonable degree of particularity and distinctness" (emphasis in original). The MPEP continues, "[s]ome latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire." MPEP also at 2173.02. The Federal Circuit also referred to the requirement for "all reasonable attempts" at claim construction and emphasized the very high bar for a finding of indefiniteness in the recent case of *Metabolite Labs, Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354 (Fed. Cir. 2004). There, the court stated, "[o]nly when a claim remains *insolubly ambiguous without a discernible meaning after all reasonable attempts at construction* must a court declare it indefinite" (emphasis added).

The claim language is analyzed in light of the specification and the teachings of the prior art, and any conclusions regarding clarity are based on the interpretation that would be made by one of ordinary skill in the art. MPEP at 2173.02. Here, the term "reaction product" is used in a usual way; that is, in such as way as to indicate to one of ordinary skill in the art that the alkaloid formulation comprises a product formed from a reaction between the reactants as opposed to one in which the reactants are present as separate species. Those of ordinary skill in the chemical arts are trained in the analysis of chemical reaction products. Here, for example, one could use vapor pressure osmometry (VPO) to determine the average molecular weight of compounds in solution and, therefore, to detect the formation of a reaction product. VPO has been employed by Applicants in other applications (*e.g.*, US 2004/0052754).

According to a "quick search" of the U.S. Patent and Trademark Office's website, conducted by the undersigned, as of today's date, the term "reaction product" appears *in the claims* of 26,270 issued U.S. patents. While there will surely be significant variability in those claims, this establishes that (1) the term "reaction product" is certainly not indefinite *per se* and (2) it is a term that those of ordinary skill in the art frequently use and routinely encounter and would, therefore, presumably readily understand. It is hard to imagine a term appearing in 26,270 issued patents if those of ordinary skill in the art did not understand what it meant. At least one patent including a very similar term – "the product of reaction of" – was the subject of litigation. In *In re Simon*, 302 F.2d 737, 133 USPQ 524 (CCPA 1962), the court considered two claims, the broadest of which read:

> 20. A cellular material which is the product of reaction of a foaming composition comprising on a perctage by weight basis, 10 to 75% castor oil, 0.1 to 5% water and the remainder meta-toluene diisocyanate.

The court found the claim invalid because, while the claim referred to three reactants, the specification disclosed no less than five reactants. The claim failed because the subcombination claimed was not adequately supported by the written description. There is no indication that the challenger or the court considered the claim indefinite, despite its coverage of a "material which *is the product of reaction of*…"

For at least the foregoing reasons, Applicants respectfully submit that the present claim 1, from which the remaining rejected claims depend, would adequately apprise one of ordinary skill in the art of its scope. This ground for rejection should be withdrawn.

Claims 19 to 20, which are discussed at pages 2-3 of the Office action, have been canceled without prejudice. Accordingly, the rejection for indefiniteness as applied to those claims is now moot.

35 U.S.C. § 101

Claims 1-22 were rejected under 35 U.S.C. § 101 "because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process" (Office action at page 3).

Of the claims pending at the time of examination, only claim 20 referred to "use of the reaction product." As noted above, claim 20 has been canceled. Applicants therefore believe this ground for rejection is now moot.

35 U.S.C. § 103(a)

Claims 1-3, 6, and 8-22 are rejected for allegedly being obvious over Kirby *et al.* (U.S. Patent No. 6,444,234; herein, "the '234 patent") in view of WO 02/40033 (herein, "the '033 application"). See the Office Action, bridging paragraph, pages 3-4.

The Examiner characterizes the '234 patent as disclosing "[p]harmaceutical compositions for the transdermal administration of a medicament" and states that the compositions can include "an active agent such as morphine" and a carrier that "comprises solvent and modifying agents" (Office action at page 4, citing the '234 patent at 5:3-5 and Example 14 at column 42). The Examiner recognizes that the '234 patent "does not explicitly teach using phosphate derivatives of tocopherol or other tocols as claimed in the instant application as solvent modifiers" (Office action at pages 4-5).

Turning to the '033 application, the Examiner states, "[a]ccording to ('033), the use of a phosphorylated electron transfer agent plays therapeutic and efficacious role in dermal

penetration" (Office action at page 5, citing '033 at 3:3-8). Various examples of classes of "electron transfer agents" are reviewed (Office action at page 5, citing '033 at 3:25-28 and 4:1-2). Significantly, regarding a carrier, the Examiner states (Office action at page 5, citing the '033 application at 4:30-33 and 5:1-6):

> As defined in ('033), the "acceptable carrier" could be classified as [a] drug, food or cosmetics … Said "acceptable carrier" can be complexed with "phosphorylated electron transfer agent" to make parenteral or enteral formulations such as tablets, powders, …

Based on the above two references, the Examiner concludes that it would have been obvious "to use the phosphate derivatives of tocopherol ('033) in the compositions of ('234) because ('033) shows that phosphate derivatives of electron transfer agents such as tocopherol phosphate derivatives *when complexed with a drug*, possess an unexpected property in exhibiting an efficacious role in dermal penetration of the therapeutically active formulation" (Office action at page 6; emphasis added).

Applicants respectfully disagree.

As noted above, based on the passage at pages 4 to 5 of the '033 application, the Examiner relies on a teaching in the art that the phosphate derivatives of electron transfer agents are complexed with a carrier that is a drug, food or cosmetic. For ease of reference, the relevant passage of the '033 application is reproduced here:

> The term "acceptable carrier" is used herein to refer to a carrier considered by those skilled in the drug, food or cosmetic arts to be non-toxic when used to treat humans, animals or plant (*sic.*) in parenteral or enteral formulations. The carrier chosen will depend on the route of administration. Ingestible formulations include tablets, capsules, powders, chewable tablets, capsules, oral suspensions, children's formulations, enteral feeds, nutraceuticals and functional foods. For a topical application, the carrier typically comprises hydrophilic substances such as water, glycerol, polyethyleneglycol, sorbitol or propanol. For example, the composition could be used as a shampoo, hair conditions, moisturizing cream or lotion or lipstick as a topical application.

Thus, contrary to the Examiner's reading of the '033 application as teaching that (a) phosphate derivatives of electron transfer agents can be combined with an acceptable carrier

and (b) the acceptable carrier could be classified as a drug (*see* the Office action at page 5, last bullet point), the '033 application defines the term "acceptable carrier" as a carrier *considered by those skilled in the drug, food or cosmetic arts* to be non-toxic. Thus, the carrier of the '033 application is an inert, non-active substance, not a drug or the like. The Examples of the '033 application are consistent with this in their use of water or a water/ethanol mixture in the compositions comprising electron transfer agents.

Certain passages in the Office action indicate that the Examiner may be taking the position that, since preparing a phosphate derivative of an electron transfer agent enhances dermal penetration, and since the carrier disclosed in the '234 patent may be one that facilitates cellular targeting, one would have been motivated to use the phosphate derivative of the electron transfer agent ('033) in combination with another drug, such as an active agent disclosed in the '234 patent, so that the phosphate derivative would improve, in some way, the delivery of the drug. However, it is the phosphorylation of the electron transfer agent that is believed to facilitate dermal penetration *of the electron transfer agent*; the '033 application suggests that phosphorylating electron transfer agents results in better dermal penetration (*see* page 3, lines 2-7). There is nothing, however, in either the '033 application, the '234 patent, or the combination of the two that suggests that one should react a phosphate derivative *of* an electron transfer agent *with* an alkaloid, as all of the present claims require. The fact that phosphate derivatives of electron transfer agents may be superior to unphosphorylated electron transfer agents is wholly separate.

In view of the foregoing, the Examiner is asked to reconsider and withdraw this ground for rejection.

Claims 4, 6, and 7 are rejected under 35 U.S.C. § 103(a) as being obvious over Schor *et al.* (U.S. Patent No. 4,369,172; "the '172 patent") in view of the '033 application (Office Action at page 7, lines 4-6).

Claims 4, 6, and 7 depend, directly and indirectly, from claim 1 which has been discussed above. Because the '033 application fails completely to suggest the reaction product of claim 1, the addition of the '172 patent cannot, for the simple additional disclosure of additional inert

carrier materials such as hydroxypropylmethylcellulose, render the subject matter of claims 4, 6, and 7 obvious. Neither the '172 patent nor the '033 application, either alone or in combination, discloses or suggests the claimed formulations containing *the reaction product* of one or more alkaloids with one or more phosphate derivatives of one or more electron transfer agents, whether or not those products are formulated for oral or buccal administration (as covered by claims 4 and 7) or are formulated as a powder or in any of the other forms recited in claim 6.

Claim 5 is rejected under 35 U.S.C. §103(a) as being unpatentable over the '172 patent in view of the '033 application and further in view of Fisher et al. U.S. Patent Application No. 2004/0234602 (the '602 application).

Claim 5 depends indirectly from claim 1, which has been discussed above, and further limits claim 1 to a formulation that includes an enteric coating. While the '602 application may disclose a composition with an enteric coating, that addition is not sufficient to cure the earlier described deficiencies of the prior art. The phosphate derivatives of the '033 application do not participate with an alkaloid to form a reaction product.

For the reasons discussed above, Applicants believe that the application is now in condition for allowance, which action is respectfully requested.

CONCLUDING FORMALITIES

A Petition for Extension of Time is being filed herewith. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: June 6, 2007

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